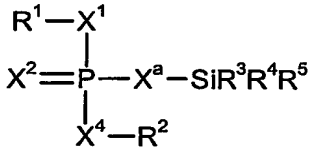
CLAIMS

1. An oligonucleotide comprising at least one internucleotide phosphorus atom protected with a group of formula $-X^aSiR^3R^4R^5$ wherein X^a represent O or S, and R^3, R^4 and R^5 each independently are optionally substituted hydrocarbyl groups, selected such that that total number of carbon atoms in R^3 plus R^4 plus R^5 is 4 or more.

2. An oligonucleotide according to claim 1, wherein the group of formula $-X^aSiR^3R^4R^5$ is a tert-butyldimethylsilyloxy group.

3. An oligonucleotide according to either of claims 1 and 2, wherein a single group of formula $-X^aSiR^3R^4R^5$ is located at the terminal internucleotide linkage.

4. An oligonucleotide according to claim 1, having the Formula (1):



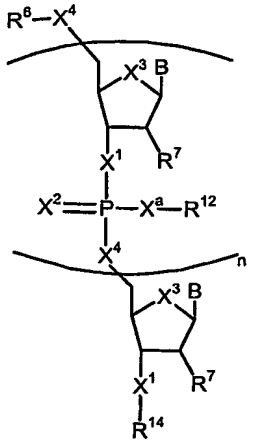
Formula (1)

wherein:
R^1 and R^2 independently are nucleoside, nucleotide or oligonucleotide moieties;
R^3, R^4 and R^5 each independently are optionally substituted hydrocarbyl groups, selected such that that total number of carbon atoms in R^3 plus R^4 plus R^5 is 4 or more;
X^a represents O or S, preferably O;
X^1 and X^4 are each independently -O-, $-CH_2-$, -S- or NR^n, where R^n represents H or C_{1-4} alkyl, preferably both of X^1 and X^4 being O; and
X^2 is O or S, preferably S.

5. An oligonucleotide according to claim 4, wherein X^1, X^a and X^4 are each O, and one of R^3, R^4 and R^5 represents a tert-butyl group, with the others representing methyl groups.

6. An oligonucleotide according to either of claims 4 and 5, wherein R^1 is a nucleotide substituted at the 3'-position by X^1, and R^2 represents an oligonucleotide substituted at the 5'-position by X^4.

7. An oligonucleotide according to claim 4, of Formula (2):



Formula (2)

wherein:

X^a for each occurrence is independently -O- or S-;

X^1 and X^4 are, independently, -O-, $-CH_2-$, -S- or NR^n, where R^n represents H or C_{1-4} alkyl;

X^2 for each occurrence is O or S;

X^3 for each occurrence is, independently, -O-, -S-, $-CH_2-$, or $-(CH_2)_2-$;

R^6 is H, an alcohol protecting group, an amino protecting group or a thio protecting group;

R^7 for each occurrence is, independently, -H, -F $-OR^8$, $-NR^9R^{10}$, $-SR^{11}$, or a substituted or unsubstituted aliphatic group, such as methyl or allyl;

R^8 for each occurrence is, independently, -H, a substituted or unsubstituted aliphatic group (e.g., methyl, ethyl, methoxyethyl or allyl), a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkyl, an alcohol protecting group, or $-(CH_2)_q-NR^xR^y$;

R^9 and R^{10} for each occurrence are each, independently, -H, a substituted or unsubstituted aliphatic group, or an amine protecting group, or R^9 and R^{10} taken together with the nitrogen to which they are attached are a heterocyclyl group;

R^{11} for each occurrence is, independently, -H, a substituted or unsubstituted aliphatic group, or a thio protecting group;

R^{12} for each occurrence is, independently, a phosphorus protecting group, provided that at least one R^{12} represents a group of formula $-SiR^3R^4R^5$, in which R^3, R^4 and R^5 are as previously defined;

R^{13} is for each occurrence is, independently, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted aryl group or a substituted or unsubstituted aralkyl group;

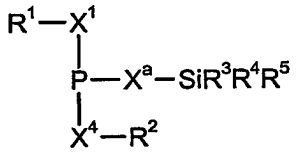
R^{14} is H a hydroxy protecting group, a thio protecting group, an amino protecting group, $-(CH_2)_q-NR^xR^y$, a solid support, or a cleavable linker attached to a solid support;

R^x and R^y are each, independently, -H, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted aliphatic

group, a substituted or unsubstituted aralkyl group, a substituted or unsubstituted heteroaralkyl group or an amine protecting group, or, R^x and R^y taken together with the nitrogen to which they are attached form a heterocyclyl group;
q is an integer from 1 to about 6;
B is -H, a natural or unnatural nucleobase, or a protected natural or unnatural nucleobase; and
n is a positive integer.

8. An oligonucleotide according to claim 7, wherein each X^1, X^3 and X^4 are O; R^6 is H or an alcohol protecting group; R^7 is H, F, OCH_3, $OCH_2CH_2OCH_3$ or O-protecting group; R^{12} is $-CH_2CH_2CN$ or tert-butyldimethylsilyl, provided at least one R^{12} is tert-butyldimethylsilyl; R^{14} is H or a cleavable linker attached to a solid support, and n is from 8 to 40.

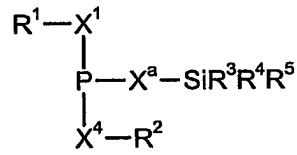
9. A process for the preparation of a compound of Formula (1) as defined in claim 4, which comprises oxidising or sulfurising a compound of Formula (3):



Formula (3)

wherein R^1, R^2, R^3, R^4, R^5, X^a, X^1 and X^4 are as defined in claim 4.

10. A compound of Formula (3):



Formula (3)

wherein R^1, R^2, R^3, R^4, R^5, X^a, X^1 and X^4 are as defined in claim 4.

11. A compound of Formula (4):

R^1-X^1-P($NR^{17}R^{18}$)-X^a-$SiR^3R^4R^5$

wherein R^1, R^3, R^4, R^5, X^a and X^1 are as defined in claim 4, and R^{17} and R^{18} are each, independently, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkyl or R^{17} and R^{18} taken together with the nitrogen to which they are bound form a heterocyclyl group.

12. A process for the preparation of a compound of Formula (1) as defined in claim 4 which comprises:
a) coupling a compound of Formula (4) as defined in claim 11, with a compound of formula R^2-X^1-H wherein R^2 and X^1 are as defined in claim 4, in the presence of an activator; and b) oxidising or sulfurising the product of step a).

13. A process for the preparation of a compound of Formula (3) as defined in claim 10 which comprises coupling a compound of Formula (4) as defined in claim 11, with a compound of formula R^2-X^1-H wherein R^2 and X^1 are as defined in claim 4, in the presence of an activator.

14. A process for the preparation of a compound of Formula (4) as defined in claim 11, which comprises reacting a compound of formula R^1-X^1-H, wherein R^1 and X^1 are as defined in claim 4 with a compound of formula $R^3R^4R^5Si$-X^a-P($NR^{17}R^{18}$)$_2$ wherein X^a, R^3, R^4, R^5, R^{17} and R^{18} are as defined in claim 5.

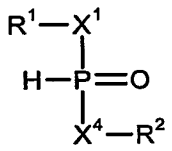
15. A process for the preparation of a compound of Formula (4) wherein X^a is O which comprises a) reacting a compound of formula R^1-X^1-H, wherein R^1 and X^1 are as defined in claim 4 and a compound of formula Z-P($NR^{17}R^{18}$)$_2$ wherein R^{17} and R^{18} are as defined in claim 11 and Z represents a leaving group, preferably a chlorine atom, to form a compound of formula R^1-X^1-P($NR^{17}R^{18}$)$_2$; b) hydrolysing the compound of formula R^1-X^1-P($NR^{17}R^{18}$)$_2$ to form a compound of formula R^1-X^1-PH(=O)($NR^{17}R^{18}$), the hydrolysis preferably taking place in the presence of a weak acid, such as tetrazole, S-ethyltetrazole, or an imidazole salt; and c) reacting the compound of formula R^1-X^1-PH(=O)($NR^{17}R^{18}$) with a silylating agent of formula Y^1-$SiR^3R^4R^5$ wherein Y^1 is a leaving group, to form the compound of Formula (4).

16. A process for the preparation of a compound of formula $R^3R^4R^5Si$-X^a-P($NR^{17}R^{18}$)$_2$ which comprises reaction of a compound of formula Z-P($NR^{17}R^{18}$)$_2$ as defined in claim 15, with a compound of formula H-X^a-$SiR^3R^4R^5$, wherein X^a, R^3, R^4, and R^5 are as defined in claim 1, preferably in the presence of a base.

17. A process for the preparation of a compound of formula $R^3R^4R^5Si\text{-}O\text{-}P(NR^{17}R^{18})_2$ wherein R^3, R^4, and R^5 are as defined in claim 1, and R^{17} and R^{18} are as defined in claim 11 which comprises:
a) hydrolysis of a compound of formula $Z\text{-}P(NR^{17}R^{18})_2$ wherein Z is as defined in claim 15 to form a compound of formula $H\text{-}O\text{-}P(NR^{17}R^{18})_2$; and
b) reaction of the product of step a) with a compound of formula $Y^1\text{-}SiR^3R^4R^5$ wherein Y^1 is a leaving group.

18. A process for the synthesis of an oligonucleotide comprising at least one internucleotide phosphorus atom protected with a group of formula $-X^1SiR^3R^4R^5$, wherein X^1 represents O or S, and R^3, R^4 and R^5 each independently are optionally substituted hydrocarbyl groups, selected such that the total number of carbon atoms in R^3 plus R^4 plus R^5 is 4 or more, which comprises reacting a silylating agent of formula $Y^1\text{-}SiR^3R^4R^5$, wherein Y^1 is a leaving group, with an oligonucleotide H-phosphonate diester.

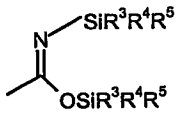
19. A process according to claim 18, wherein the oligonculeotide H-phosphonate diester is a compound of Formula (7):



wherein
R^1, R^2, X^1 and X^4 are as defined in claim 4.

20. A process according to either of claims 18 or 19, wherein R^1 is a nucleotide substituted at the 3'-position by X^1, R^2 represents an oligonucleotide substituted at the 5'-position by X^4, and X^1 and X^4 are both O.

21. A process according to any one of claims 18 to 20, wherein the silylating agent is a group of formulae:

 or $(R^3R^4R^5Si)_2NH$

22. A process according to any one of claims 18 to 21, wherein one of R^3, R^4 and R^5 represents a tert-butyl group, with the others representing methyl groups.

23. A process for the preparation of a deprotected oligonucleotide which comprises a) assembling an oligonucleotide compound comprising at least one internucleotide phosphorus atom protected with a group of formula $-X^aSiR^3R^4R^5$ wherein X^a, R^3, R^4 and R^5 are as defined in claim 1, and b) removing the $SiR^3R^4R^5$ groups.